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14. ABSTRACT: Tumor biology is a recognized determinant of tumor behavior, including growth rate, motility and metastatic potential, and therapeutic resistance. This project was funded to investigate the regulation and expression of an excellent marker for aggressive breast tumors: RhoC-GTPase. When overactive, RhoC transforms mammary epithelial cells into a highly motile and invasive phenotype. We hypothesize that RhoC overexpression may be regulated by the transcription factor NF-kappa B and that at the same time RhoC is overexpressed the tumor also acquires therapy resistance. The objective of this study is to utilize existing breast cancer cohorts with tumor tissue and treatment response data available to assess the correlation between NF-kappa B and RhoC, individually and in combination, to treatment response. The specific aims of the project are to determine 1) if RhoC and NF-kappa B are correlated; 2) if RhoC and NF-kappa B are associated, individually and in combination, with aggressive breast cancer; and 3) if NF-kappa B and RhoC are associated with therapy resistance.					
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INTRODUCTION

This study was funded to assess the relationship of RhoC and NF-kappa B to aggressive, metastatic, and therapy-resistant breast cancer. Inflammation is currently being considered a key component of cancer initiation and progression. [1] Many proinflammatory stimuli act through an NF-kappa B dependent signaling pathway. It is likely that RhoC, which is recognized as an important marker of breast cancer, aggressiveness is also regulated by NF-kappa B.

The tumor microenvironment is exceptionally critical in our understanding of cancer development. Recent research suggests that chronic inflammation is triggered during tumor growth. The tumor associated inflammation contributes greatly to the tumor microenvironment and perhaps even to tumor macroenvironment. Tumor-associated macrophages (TAMs) secrete numerous signaling molecules that interact with tumor and stromal cells. Secretion of TNF- α by TAMs activates NF-kappa B within the tumor cell through the receptor tyrosine kinase pathway.

Rho-GTPases are members of the Ras-superfamily. Activation of Rho promotes both the bundling of actin filaments with myosin II filaments into stress fibers and the clustering of integrins and associated proteins to form focal contacts. [2] Experiments conducted within the Merajver laboratory have shown an active role for RhoC in rearrangement of the cytoskeleton in cell motility and invasion.

We hypothesize that NF-kappa B is a transcription factor for the RhoC gene and leads to overexpression of cellular RhoC protein. As more is learned about these tumor markers, the potential exists for improved clinical diagnosis, prognosis, and treatment. The purpose of the study is to understand the regulation of RhoC gene expression in an epidemiological setting. A clear understanding of the genetic and cellular mechanisms involved in modulating a highly metastatic phenotype is expected to aid in diagnosis and treatment.

The scope of this work includes the identification and collection of patient information from Henry Ford Health system (HFHS). HFHS is an integrated health system that offers a diverse, population-based patient population from which strong epidemiologic studies can be built. Patient information, including diagnostic and recurrence data, will be combined with gene expression data. Molecular and statistical analysis will occur in collaboration with the University of Michigan.

BODY

In the second 12 months of the project, we projected that we would conduct the study tumor microarray analyses. Below are the objectives from the original statement of work.

- Task 3.*
- To conduct tumor microarray analyses
 - a. Write laboratory procedures manual
 - b. Prepare TMA
 - c. Interpret and quantify TMA results
 - d. Enter laboratory data results into database

The complete dataset (abstracted medical record data with TMA data) is expected to be established within the next 6 months. At that time we will be able to begin the analysis of the data for key results. Although case identification and key patient level information had already been collected, it was decided that the time and effort was available to conduct a more systematic medical record abstraction. A formal data collection codebook (Appendix A) and data collection instrument (Appendix B) were developed. The data collection instrument was developed into an ACCESS database form to which TMA can be easily and efficiently added. In addition, it was decided after biostatistical consult to expand the years of patient accrual as well as the eligible tumor stages. This will ensure that adequate power is available for the final analyses.

Other research activities, supported in part by funding from this grant, have included working with population data for the Arab-American community in Detroit. Arab women have been reported to have an increased incidence of inflammatory breast cancer (IBC), a particularly aggressive form of breast cancer. RhoC has been shown to be amplified in inflammatory breast cancer and may likely be the key to IBC's aggressive phenotype. [3] Ms. Alford presented a poster on breast cancer in Arab-American women during the 2005 San Antonio Breast Cancer Symposium. [4] This poster presentation was also given at the Henry Ford Health System Annual Research Symposium where it was selected as a winner.

KEY RESEARCH ACCOMPLISHMENTS

- Development of data collection instrument and codebook
- Creation of an ACCESS form for data entry
- Expansion of study sample

REPORTABLE OUTCOMES

Reportable outcomes are expected for the next review.

CONCLUSIONS

Exciting research has surfaced in the past year regarding the tumor microenvironment and breast cancer metastasis. Areas which our genes of interest are likely to play a significant role. Despite this, no one else is currently investigating our genes of interest and their role in an aggressive breast cancer phenotype. As clinical oncology looks more to targeted therapy for treatment options, our work will hopefully be able to provide valuable insight for drug development.

REFERENCES

- [1] Lu H, Ouyang W, Huang C. Inflammation, a key event in cancer development. *Mol Cancer Res* 2006;4(4):221-33.
- [2] Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. *Molecular Biology of the Cell* 4th edition. Garland Science 2002 New York, NY.

- [3] van Golen KL, Davies S, Wu ZF et al. A novel putative low-affinity insulin-like growth factor-binding protein, LIBC (lost in inflammatory breast cancer) and RhoC GTPase correlate with the inflammatory breast cancer phenotype. Clin Cancer Res 1999;5:2511-9.
- [4] Hensley Alford S, Schwartz K, Soliman A, Gruber S, Douglas JA, Johnson CC, Merajver SD. "Breast cancer characteristics at diagnosis among Arab-American women compared to European- and African-American women in the Detroit SEER registry." San Antonio Breast Cancer Symposium 2005

APPENDICES

- A: Data collection instrument coding book
B: Data collection instrument

APPENDIX A: Data Collection Codebook

Significance of Pathways Leading to RhoC Overexpression in Breast Cancer

Coding Manual for the Data Collection Instrument(DCI)

E1. Eligibility Information

E1.1 Date of Diagnosis

DATA ELEMENT:	Date of Definitive Surgery
DEFINITION:	The date of the patient's definitive surgery, defined as surgery associated with the first positive pathology report.
SOURCE DOCUMENT:	Medical record: pathology report.
CODE RANGE:	Record as MONTH, DAY, YEAR (MM / DD / YYYY) MONTH 01-12 DAY 01-31 YEAR 1996–2003 Code complete (4-digit) year.
DIRECTIVES:	Required. Enter the date of the patient's breast cancer diagnosis. If month is unknown enter MM = 06. If day is unknown enter DD = 15.

E1.2 Invasive Malignancy

DATA ELEMENT:	Was the primary breast cancer diagnosis an invasive malignancy?
DEFINITION:	To determine whether the primary breast cancer was an invasive malignancy.
SOURCE DOCUMENT:	Medical Record: pathology report.
CODE RANGE:	01 – 09
DIRECTIVES:	Required. If the primary breast cancer diagnosis was an invasive malignancy enter code 01 and go to E1.3. If the primary breast cancer diagnosis was not an invasive malignancy enter code 02. Patient is ineligible – end of data collection. If the primary breast cancer diagnosis is unknown enter code 09. These cases will be reviewed.

E1.3 Cancer laterality

DATA ELEMENT:	Was the primary breast cancer bilateral?
DEFINITION:	To determine laterality of the primary breast cancer.
SOURCE DOCUMENT:	Medical Record
CODE RANGE:	01 – 02
DIRECTIVES:	Required. If the primary breast cancer was bilateral enter code 01. Patient is ineligible – end of data collection. If the primary breast cancer was not bilateral enter code 02

E1.3.1 Side of the breast cancer

DATA ELEMENT:	Side of breast cancer
DEFINITION:	To determine laterality of the unknown primary breast cancer.
SOURCE DOCUMENT:	Medical Record
CODE RANGE:	01 – 02
DIRECTIVES:	Required.

E1.4 Stage grouping

DATA ELEMENT:	Stage grouping
DEFINITION:	Stage of disease reported for the primary breast cancer
SOURCE DOCUMENT:	Pathology report.
CODE RANGE:	01 to 09
DIRECTIVES:	Required. Combining TNM data to determine stage Enter 00: Stage 0: T _{1s} , N ₀ , M ₀ Ineligible – end of data collection Enter 01: Stage I: T ₁ , N ₀ , M ₀ Enter 02: Stage IIA: T ₀ , N ₁ , M ₀ T ₁ , N ₁ , M ₀ T ₂ , N ₀ , M ₀ Enter 03: Stage IIB: T ₂ , N ₁ , M ₀ T ₃ , N ₀ , M ₀ Enter 04: Stage III: T ₀ , N ₂ , M ₀ Ineligible – end of data collection T ₁ , N ₂ , M ₀ Ineligible – end of data collection T ₂ , N ₂ , M ₀ Ineligible – end of data collection T ₃ , N ₁ , M ₀ Ineligible – end of data collection T ₃ , N ₂ , M ₀ Ineligible – end of data collection T ₄ , any N, M ₀ Ineligible – end of data collection Any T, N ₃ , M ₀ Ineligible – end of data collection Enter 05: Stage IV: Any T, Any N, M ₁ Ineligible – end of data collection Enter 09: Unknown: T _x or N _x or M _x Ineligible – end of data collection

E1.5 Source of stage

DATA ELEMENT:	Source of primary breast cancer stage information.
DEFINITION:	Was the primary diagnosed pathologically or clinically?
SOURCE DOCUMENT:	Pathology report, medical record.
CODE RANGE:	00 – 06
DIRECTIVES:	Required. The codes for source of stage information are arranged in numerical order from the most important (00) to the least important (06). Select the first and therefore most important from the list that is the source of the stage information. If the source of the stage information was based on pathology report then enter 00. If the source of the stage information was based on pathology report, referred to but not in the chart then enter 01. If the source of the stage information was based on MD notes from hematology/oncology then enter 03. If the source of the stage information was based on MD notes, primary care physician then enter 04. If the source of the stage information was based on MD notes, other then enter 05. If the source of the stage information was based on any other method enter 06 and specify.

E1.6 First episode of malignant breast cancer

DATA ELEMENT:	Was this the patient's first episode of malignant breast cancer?
DEFINITION:	To determine if this was the patient's first episode of malignant breast cancer.
SOURCE DOCUMENT:	Medical Record
CODE RANGE:	01 – 09
DIRECTIVES:	Required. If this was the patient's first episode of malignant breast cancer enter code 01 go to E1.7. If this was not the patient's first episode of malignant breast cancer enter code 02. Patient is ineligible – end of data collection.

E1.7 Other clinically active malignancy

DATA ELEMENT:	Was the patient diagnosed with any other clinically active malignancy?
DEFINITION:	To determine if the patient was diagnosed with any other clinically active malignancy.
SOURCE DOCUMENT:	Medical Record
CODE RANGE:	01 – 09
DIRECTIVES:	Required. If the patient was diagnosed with any other clinically active malignancy enter code 01. Patient is ineligible – end of data collection. If the patient was not diagnosed with any other clinically active malignancy enter code 02

E1.8 Age at Diagnosis

DATA ELEMENT:	Patient age
DEFINITION:	The patient's age in years (at time of diagnosis).
SOURCE DOCUMENT:	Medical record
CODE RANGE:	3 DIGIT NUMERIC
DIRECTIVES:	Required. Enter up to 3 digit age in years.

1. Demographic Information

1.1. Patient ID

DATA ELEMENT:	Patient Identification Number
DEFINITION:	The five-digit identification number.
SOURCE DOCUMENT:	The identification number is assigned, use the patient list.
CODE RANGE:	The digits are a unique random number.
DIRECTIVES:	Required. This field should never be left blank and is recorded on each sheet.

1.2. Date of Birth

DATA ELEMENT:	Date of birth
DEFINITION:	The month and year of the patient's date of birth.
SOURCE DOCUMENT:	Medical record
CODE RANGE:	MM /YYYY
DIRECTIVES:	Required.

1.3. Ethnicity

DATA ELEMENT:	Patient's ethnicity
DEFINITION:	Ethnicity as reported to or record by care providers.
SOURCE DOCUMENT:	Medical Record
CODE RANGE:	00,01,09
DIRECTIVES:	<p>If the medical record indicates that the patient is Hispanic then code 01. Hispanic is defined as a person of Mexican, Puerto Rican, Cuban, South American (except Brazil) or Central American origin, regardless of race.</p> <p>If the medical record indicates that the patient is not Hispanic then code 00.</p>

1.4. Race

DATA ELEMENT:	Patient's race
DEFINITION:	The one race that the patient reported to or is recorded by the care providers.
SOURCE DOCUMENT:	Medical Record
CODE RANGE:	01 – 04
DIRECTIVES:	<p>If the race listed in the medical record is white code 01. White refers to people having origins in any of the original peoples of Europe, the Middle East or North Africa. However, if they are of Arab decent then code 03 and list the country of origin.</p> <p>If the race listed in the medical record is African-American code 02. African-American refers to any of the black racial groups of Africa including Caribbean-Americans.</p> <p>If the race in the medical record is not included in the above list code 04 and specify on the line provided.</p> <p>If more than once race is recorded use the following guidelines. If race is recorded as white and another race, code as the other race. If a women's race is recorded as Hawaiian and another race, code as Hawaiian. Otherwise code as the first non-white race listed. This hierarchy is based on the instructions provided in the SEER coding manual (1998).</p>

2. Personal History

2.1. Medical History

DATA ELEMENT:	History of other cancers and cardiovascular related diseases
DEFINITION:	Diseases of interest noted at the time of diagnosis
SOURCE DOCUMENT:	Medical record
CODE RANGE:	None
DIRECTIVES:	<p>Record the history of any prior cancers and specify the cancers in the space provided. Non-melanoma skin cancers do not need to be recorded and if the patient has a history of a prior breast cancer then she is ineligible.</p> <p>Cardiovascular diseases of interest include heart disease, cerebrovascular disease, hypertension, and hypercholesterolemia.</p>

2.2. Family History

DATA ELEMENT:	Family members with cancer
DEFINITION:	Family history of cancer
SOURCE DOCUMENT:	Medical record
CODE RANGE:	None
DIRECTIVES:	Record “yes or no” whether the patient reported a history of breast, ovarian, or other cancer. For each cancer reported, record if a first-degree or non-first degree relative was diagnosed. Record both is appropriate. In the case of an “other” cancer then specify the type of cancer.

2.3. History of in situ disease

DATA ELEMENT:	LCIS or DCIS diagnosis
DEFINITION:	Patient history of LCIS/DCIS prior, concurrent, and following invasive diagnosis.
SOURCE DOCUMENT:	Medical record
CODE RANGE:	NA
DIRECTIVES:	<p>If patient has a history of DCIS and/or LCIS prior to their invasive diagnosis, then circle the “X” associated with the diagnosis. If no history is noted then circle the “X” for the “No”.</p> <p>Record in the same manner for DCIS and/or LCIS noted at the time of diagnosis.</p> <p>If patient has a diagnosis of LCIS and/or DCIS following the invasive diagnosis but prior to a recurrent invasive diagnosis then note in 2.3.3.</p>

2.4. Smoking Status

DATA ELEMENT:	Smoking status
DEFINITION:	Patient history of smoking
SOURCE DOCUMENT:	Medical record
CODE RANGE:	01-04
DIRECTIVES:	<p>If patient used to smoke and has successfully quit, enter 01.</p> <p>If patient currently smokes, enter 02.</p> <p>If patient has never smoked, enter 03.</p> <p>If smoking history is unknown, enter 04.</p>

2.5. Marital status

DATA ELEMENT:	Marital status
DEFINITION:	Is the patient currently married, divorced/widower, or separated/single/never married
SOURCE DOCUMENT:	Medical record
CODE RANGE:	01 – 04
DIRECTIVES:	If patient is married at the time of diagnosis code 01. If patient is divorced or widowed at the time of diagnosis code 02. If patient is separated, single or has never been married then code 03. If there is no mention in the medical record then code 04.

2.6. Gravidity

DATA ELEMENT:	Gravidity
DEFINITION:	Number of times patient has been pregnant.
SOURCE DOCUMENT:	Medical record
CODE RANGE:	00-99
DIRECTIVES:	If the patient has never been pregnant then code 00. If the patient has been pregnant then use a two digit code to record the number of pregnancies. If there is no mention of the patient's pregnancy history then code 99.

2.7. Parity

DATA ELEMENT:	Parity
DEFINITION:	Number of live births
SOURCE DOCUMENT:	Medical record
CODE RANGE:	00-99
DIRECTIVES:	If the patient has never had a live birth then code 00. If the patient has had at least one live birth then use a two digit code to record the number of live births. If there is no mention of the number of live births then code 99.

2.8. Age of first pregnancy

DATA ELEMENT:	Patient age
DEFINITION:	Age the patient was at the time of her first pregnancy
SOURCE DOCUMENT:	Medical record
CODE RANGE:	2 digit numeric
DIRECTIVES:	Use a two digit code to record the age of the patient at the time of her first pregnancy

2.9. Age at menarche

DATA ELEMENT:	Patient age
DEFINITION:	The patient's age at menarche
SOURCE DOCUMENT:	Medical record
CODE RANGE:	2 digit numeric
DIRECTIVES:	Enter the age of the patient when she reported having started menstruating. If there is no mention then enter 99.

2.10. Age at menopause

DATA ELEMENT:	Patient age
DEFINITION:	The patient's age at menopause
SOURCE DOCUMENT:	Medical record
CODE RANGE:	2 digit numeric
DIRECTIVES:	If the patient is not yet menopausal then enter code 00. If the patient is currently perimenopausal then enter 01. If the patient has experienced menopause then enter a two digit code for the patient's age at menopause.

2.11. Type of menopause

DATA ELEMENT:	Type of menopause
DEFINITION:	Menopause can be surgical (removal of ovaries), natural, or chemical.
SOURCE DOCUMENT:	Medical record
CODE RANGE:	01-04
DIRECTIVES:	If the patient had a natural menopause then code 01. If the patient's menopause was due to removal of her ovaries then

code 02.

If the patient's menopause was due to taking drugs, such as prior chemotherapy, then code as 03.

If there is no mention of the cause of the woman's menopause then code 04.

2.12. History of hormone replacement therapy

DATA ELEMENT:	History of use of hormone replacement therapy?
DEFINITION:	Prior or current use of hormone replacement therapy recorded as ever/never
SOURCE DOCUMENT:	Medical record
CODE RANGE:	01-03
DIRECTIVES:	<p>If the patient has a history of or is currently taking hormone replacement therapy then code 01.</p> <p>If the patient has never taken hormone replacement therapy then code 02.</p> <p>If there is no mention of the patient's history of hormone replacement therapy then code 03.</p>

2.13. History of oral contraceptives

DATA ELEMENT:	History of oral contraceptive use?
DEFINITION:	Prior or current use of oral contraceptives recorded as ever/never
SOURCE DOCUMENT:	Medical record
CODE RANGE:	01-03

2.14. Weight at diagnosis

DATA ELEMENT:	Weight at diagnosis
DEFINITION:	Weight of patient at or close to diagnosis
SOURCE DOCUMENT:	Medical record
CODE RANGE:	<999
DIRECTIVES:	Record the weight of the patient at the time of diagnosis (within 3 months prior to or following the diagnosis)

2.15. Height at diagnosis

DATA ELEMENT:	Height at diagnosis
DEFINITION:	Height of patient
SOURCE DOCUMENT:	Medical record
CODE RANGE:	<999
DIRECTIVES:	Record the height of the patient closest to diagnosis but any height in the chart is acceptable.

3. Breast Cancer Abstract

3.1 Tumor size

3.1.1 Presence of a report of tumor size

DATA ELEMENT:	Report of pathologic tumor size.
DEFINITION:	A yes-no response as to whether the tumor size is reported in the medical record or pathology report.
SOURCE DOCUMENT:	Pathology reports. Alternatively medical record if pathology report is missing
CODE RANGE:	01 – 02
DIRECTIVES:	Enter 01 if the source document contains a measurement of the size of the tumor. Go to section 3.1.2. Enter 02 if the source document contains no measurement of the tumor size. Skip to section 3.2.

3.1.2 Tumor size

DATA ELEMENT:	Measurement of the tumor size
DEFINITION:	Documentation of size of tumor within the specimen based on pathology, surgical procedure, biopsy, mammography or clinical examination.
SOURCE DOCUMENT:	Pathology report, medical record, operative report; discharge summary
CODE RANGE:	NUMERICAL VALUE
DIRECTIVES:	If no primary tumor, record “000.00”. The hierarchy for sources for tumor size information is the following: 1) pathology report, 2) operative report, 3) physical examination and 4) mammography. Read the entire pathology report before recording any tumor size. Record the tumor size reported in the “Summary” or “Diagnosis” section of a pathology report or other record in preference to other measurements. When no tumor size is reported in

such a section, record the tumor size reported in the gross pathology section in preference to the tumor size reported in the microscopic pathology section. If the microscopic section contains the only tumor size report, then use the microscopic measurement. Code the tumor size before any neoadjuvant therapy (radiation, chemotherapy, hormonal therapy or immunotherapy). If there was neoadjuvant therapy then you will need to record the clinical or mammographic tumor size. You may also need to modify the tumor size reported in the summary or gross section of the report if the microscopic report indicates that the tumor contains ductal carcinoma *in situ* and that indication is not reflected in the tumor size reported in the summary or gross section (*i.e.*, if the tumor size reflects more than just the invasive component -- see below).

Exclude measurements of ductal carcinoma *in situ* from the total tumor size measurement. The microscopic section of the pathology report may indicate that the total tumor size includes a DCIS component, in which case the tumor size should be reduced by the largest DCIS dimension or multiplied by (1-fraction DCIS). For example, a 1 cm tumor that includes 0.2 cm DCIS, or is reported as 20% DCIS, should be recorded as 0.8 cm diameter.

If more than one dimension is given for a tumor or piece of a tumor, record the largest dimension.

If there is more than one piece of the tumor, add the largest dimensions of all the pieces.

If there is more than one tumor, record the size for the largest tumor (including adding its pieces as described above).

Tumor size should be recorded from the procedure that reports the largest tumor when all of the pieces from that procedure are added together. Do not add pieces together from different procedures.

Report all measurements in the units given in the record. Tumor sizes are usually reported in centimeters (cm), but may be reported in millimeters (mm), inches (in. or "), or some other units. If no units are explicitly stated, write "none" in the space provided for "other units."

If the tumor size is reported as "too small to measure" or some similar description, then record the exact words of the description in the units blank of the "other" category.

Enter "x" in blanks that do not apply. For example, a tumor with total diameter reported as 2 cm would be coded xx2.xx. A tumor with total diameter reported as 2.0 cm would be coded xx2.0x.

To convert tumor sizes to comparable units in order to add pieces together or to decide which tumor is largest, use the following conversions: 10 mm = 1 cm; 2.54 cm = 1 inch. Always record the tumor size in the units reported.

The importance of collecting tumor size individually and not just as a

component of stage was based on the following articles that demonstrated that tumor size was an important long-term prognostic indicator.

Gebauer G, Fehm T, Lang N, Jager W. Tumor size, axillary node status and steroid receptor expression in breast cancer: prognostic relevance 5 years after surgery. *Breast Cancer Res Treat* 2002 75:167-73.

Hatteville L, Mahe C, Hill C. Prediction of the long-term survival in breast cancer patients according to the present oncological status. *Statist Med* 2002;21:2345-54.

Wollgren A, Bonetti M, Gelber RD, Goldhirsch A, et al. Risk factors for locoregional recurrence among breast cancer patients: results from the international breast cancer study group trials I through VII. *J Clin Oncol* 2003;21:1205.

3.1.2.1 Tumor size units

DATA ELEMENT:	Tumor size units
DEFINITION:	Documentation of tumor size units of measurement based on pathology, surgical procedure, biopsy, mammography or clinical examination.
SOURCE DOCUMENT:	Pathology report, medical record, operative report; discharge summary
CODE RANGE:	01 – 04 UNITS OF MEASUREMENT
DIRECTIVES:	Required. Enter reported tumor size units of measurement use the following codes; 01 = Centimeters (cm) 02 = Millimeters (mm) 03 = Inches (in or “) 04 = Other units; specify _____

3.2 Histology

DATA ELEMENT:	Histology
DEFINITION:	Code of histologic type of breast cancer.
SOURCE DOCUMENT:	Pathology reports. Alternatively medical record if pathology report is missing.
CODE RANGE:	01 to 99
DIRECTIVES:	Enter 01 if the source document reports a diagnosis of infiltrating ductal carcinoma (ICD-0 code 8500). Enter 02 if the source document reports a diagnosis of infiltrating

lobular carcinoma (ICD-O codes 8520 or 8521) .

Enter 03 if the source document reports a diagnosis of an infiltrating ductal and lobular carcinoma (ICD-O code 8523).

Enter 04 if the source document reports a diagnosis of a tumor, without specification of infiltrating ductal or lobular carcinoma (ICD-O code 8010).

Enter 05 if the source document reports a diagnosis of an adenocarcinoma, including unspecified, mucinous or tubular tumors (ICD-O codes 8140, 8211, or 8480).

Enter 06 if the source document reports a diagnosis of breast cancer other than those listed in codes 01 through 05 and specify the histologic type.

Enter 99 if the source document does not report a diagnosis of breast cancer.

Record the histology in the pathology report in preference to the medical record if the two disagree.

Record the histology based on the largest tumor specimen, whether from a definitive surgery or from a biopsy.

3.3 *Histologic grade*

DATA ELEMENT:	Histologic grade
DEFINITION:	Results of test of growth pattern and features of differentiation. If a tumor grade is specified, but it is not indicated whether it is a histologic or nuclear grade (e.g., “invasive ductal carcinoma, grade I”), assume that it is a histologic grade.
SOURCE DOCUMENT:	Pathology report or medical record.
CODE RANGE:	01 = Grade 1 (well differentiated) 02 = Grade 2 (intermediate or moderately differentiated) 03 = Grade 3 (poorly differentiated) 04 = Grade 4 (undifferentiated, anaplastic) 09 = CELL TYPE NOT DETERMINED OR NOT STATED
DIRECTIVES:	Required. Enter 09 if there is documentation that the test was not performed or if there is no documentation pertaining to histologic grade. Record the grade based on the pathology report in preference to the medical record if the two disagree. Record the grade based on definitive surgery in preference to the biopsy, if the two disagree. The histologic grade should be coded on the basis of the largest specimen when based on biopsy. For example, if an incisional

biopsy follows a needle biopsy, the histologic grade should be coded on the basis of the results of the incisional biopsy.

If the histologic grade is given as a range of grades, then code as the highest value in the range.

3.4 Definitive surgical procedure

DATA ELEMENT: Definitive surgical procedure.

DEFINITION: The procedure related to the principal diagnosis or the procedure performed for definitive purposes.

SOURCE DOCUMENT: Medical record, operative report

CODE RANGE: 00 – 98

DIRECTIVES: Required

A lumpectomy includes an excisional biopsy and removal of the tumor without the remaining unaffected breast tissue.

A partial / less than total mastectomy includes segmental mastectomy, quadrantectomy, tylectomy, wedge resection, nipple resection, or partial mastectomy NOS.

A subcutaneous mastectomy is the removal of breast tissue without the nipple and areolar complex or overlying skin.

A total or simple mastectomy removes all breast tissue, the nipple and areolar complex. An axillary dissection is not done.

A modified radical mastectomy removes all breast tissue, the nipple, the areolar complex and variable amounts of breast skin and may or may not include a portion of the pectoralis major muscle. The procedure involves an en bloc resection and dissection of the axilla.

A radical mastectomy removes all breast tissue, the nipple, the areolar complex and variable amounts of breast skin, pectoralis major and minor muscles. The procedure involves an en bloc axillary dissection.

An extended radical mastectomy removes all breast tissue, the nipple, the areolar complex and variable amounts of breast skin and pectoralis major and minor muscles. The procedure involves an en bloc axillary dissection and removal of internal mammary nodes.

If a woman participated in a blinded clinical trial involving surgery and the specifics of the type of surgery that she received are unknown then code as 98.

3.5 Date of definitive surgery

DATA ELEMENT:	Date of Definitive Surgery
DEFINITION:	The date of the patient's definitive surgery, defined as whatever surgery was coded in section 3.4.
SOURCE DOCUMENT:	Medical record.
CODE RANGE:	Record as MONTH, DAY, YEAR (MM / DD / YYYY) MONTH 01-12,99 DAY 01-31,99 YEAR 1996-2003, 9999 Code complete (4-digit) year.
DIRECTIVES:	Required. Enter the date of the patient's definitive surgery. Only enter "default codes" after you have verified that a date is not available. If month is unknown enter MM = 06. If day is unknown enter DD = 15.

3.5.1 Pathology number for surgery

DATA ELEMENT:	Pathology number
DEFINITION:	The number from the pathology report of the most definitive surgery
SOURCE DOCUMENT:	Pathology report
CODE RANGE:	Numeric
DIRECTIVES:	Report the pathology number recorded on the pathology report associated with the most definitive surgery.

3.6 Surgical Margins

DATA ELEMENT:	Surgical margins
DEFINITION:	In the final pathology report were the margins histologically clear of malignancy.
SOURCE DOCUMENT:	Pathology report
CODE RANGE:	01 – 03
DIRECTIVES:	If there is no evidence of any malignancy at the margins then code as 01 and skip to 3.7. If there is evidence of macroscopic or microscopic invasive or in-situ malignancy at the margins then code as 02. If the pathology report does not provide sufficient information to determine whether the margins are clear then code as 03 and skip to

3.7.

3.6.1 Type of malignancy at surgical margins

DATA ELEMENT:	Type of malignancy at margins
DEFINITION:	Whether invasive and / or in-situ cancer is present at the surgical margins
SOURCE DOCUMENT:	Pathology report
CODE RANGE:	Y/N
DIRECTIVES:	<p>Indicate 'Y' if there is evidence of invasive malignancy at the margins. Invasive malignancies may be indicated by the following terms: invasive malignancy: malignant, invasive, infiltrating. Otherwise indicate 'N'.</p> <p>Indicate 'Y' if there is evidence of an in-situ malignancy at the margins. The following terms indicate that the tumor is an in-situ malignancy: carcinoma in situ, Stage 0, TIS, DCIS (ductal carcinoma in-situ), LCIS (lobular carcinoma in-situ), confined to epithelium, intracystic non-infiltrating, intraductal, intra-epidermal, intra-epithelial, involvement up to but not including the basement membrane, lobular neoplasia, lobular noninfiltrating, noninfiltrating, noninvasive, papillary non-infiltrating, papillary intraductal, AIS (adenocarcinoma-in-situ) or ACIS (adenocarcinoma-in-situ).</p>

3.7 Other surgeries

DATA ELEMENT:	Dates, Pathology codes, Pathology content
DEFINITION:	Listing of other surgeries associated with treatment of the tumor
SOURCE DOCUMENT:	Medical record
CODE RANGE:	Various
DIRECTIVES:	<p>For surgeries other than the definitive surgery, list the date of surgery, the type of surgery (codes below), the pathology code associated with the tissue collected during the surgery, and whether malignant cells were identified in either lymph node or tumor specimens collected.</p> <p>Surgery codes for this section include: 01 = biopsy 02 = re-excision 03 = axillary node dissection</p>

3.8 Axillary node evaluation

3.8.1 Presence of a report of axillary node evaluation

DATA ELEMENT:	Axillary node evaluation
DEFINITION:	The procedure used to characterize lymph node status.
SOURCE DOCUMENT:	Medical record
CODE RANGE:	01 to 04
DIRECTIVES:	<p>Enter 01 if the source document contains a specific indication that an axillary node evaluation was performed.</p> <p>Enter 02 if the source document contains a specific indication that a sentinel node evaluation was performed. Enter 02 in preference to 01, even if a full axillary node dissection was performed subsequent to the sentinel node evaluation.</p> <p>Enter 03 if the source document specifically indicates that no axillary node evaluation was performed. Skip to number 3.9.</p> <p>Enter 04 if the source document contains no mention of axillary node evaluation. Skip to number 3.9.</p>

3.8.2 Axillary status, number of nodes

DATA ELEMENT:	Number of regional lymph nodes removed and examined.
DEFINITION:	Number of lymph nodes removed and examined.
SOURCE DOCUMENT:	Medical record.
CODE RANGE:	01-99
DIRECTIVES:	<p>Required</p> <p>Record the number of lymph nodes removed and examined by the pathologist. Add together all nodes examined during all breast cancer procedures, including sentinel node evaluation.</p> <p>If there is documentation that nodes were examined but the exact number is not specified, code "99".</p>

3.8.3 Number of positive nodes

DATA ELEMENT:	Number of regional lymph nodes <u>positive</u>
DEFINITION:	Number of nodes examined that had breast cancer present
SOURCE DOCUMENT:	Pathology report.
CODE RANGE:	00–99
DIRECTIVES:	Required. Record the number of lymph nodes that had breast cancer present (positive nodes). Add together the number of positive nodes from all breast cancer procedures, including sentinel node evaluation. If there is documentation that no nodes were positive, record “00”. If there is documentation that some nodes were positive but the exact number is not specified, record “99”.

3.9 *Estrogen receptor protein*

DATA ELEMENT:	ESTROGEN RECEPTOR PROTEIN (ERP): TEST RESULTS
DEFINITION:	Results of estrogen receptor protein test
SOURCE DOCUMENT:	Pathology report.
CODE RANGE:	00 = Test not done (documented) 01 = Positive test result 02 = Negative test result 03 = BORDERLINE TEST RESULT 08 = Ordered but results not in chart 09 = Unknown or no information
DIRECTIVES:	Required. Use the largest tumor piece to determine estrogen receptor status. Code “TEST NOT DONE (DOCUMENTED)” if there is documentation that the test was not performed. Code ”UNKNOWN OR NO INFORMATION” if there is no documentation pertaining to ERP. Code “POSITIVE TEST RESULTS” if the test is characterized as “FAVORABLE” or “HIGH”. Code “NEGATIVE TEST RESULTS” if the test is characterized as “UNFAVORABLE” or “LOW”. Code “BORDERLINE TEST RESULTS” if the test is characterized as “INTERMEDIATE”. Whether the test is positive, negative or borderline should be based on lab-specific determination of normal range as noted in the

laboratory report.

3.10 Progesterone receptor protein

DATA ELEMENT:	PROGESTERONE RECEPTOR PROTEIN: TEST RESULTS
DEFINITION:	Results of progesterone receptor protein test
SOURCE DOCUMENT:	Pathology report.
CODE RANGE:	00 = Test not done (documented) 01 = Positive test result 02 = Negative test result 03 = BORDERLINE TEST RESULT 08 = Ordered but results not in chart 09 = Unknown or no information
DIRECTIVES:	Required. Use the largest tumor piece to determine progesterone receptor status. Code "TEST NOT DONE (DOCUMENTED)" if there is documentation that the test was not performed. Code "UNKNOWN OR NO INFORMATION" if there is no documentation pertaining to progesterone receptor protein. Code "POSITIVE TEST RESULTS" if the test is characterized as "FAVORABLE" or "HIGH". Code "NEGATIVE TEST RESULTS" if the test is characterized as "UNFAVORABLE" or "LOW". Code "BORDERLINE TEST RESULTS" if the test is characterized as "INTERMEDIATE". Whether the test is positive, negative or borderline should be based on lab-specific determination of normal range as noted in the laboratory report.

3.11 *Her2/neu Status*

DATA ELEMENT:

DEFINITION: Results of

SOURCE DOCUMENT: Pathology report.

CODE RANGE: 00 = Test not done (cases <1999) **skip to 4**
01 = 1+
02 = 2+
03 = 3+
04= negative
08 = Ordered but results not in chart
09 = Unknown or no information

DIRECTIVES: Required.

3.11.1 *Her2/neu test type*

DATA ELEMENT: Test used for Her2/neu categorization

DEFINITION: Results of progesterone receptor protein test

SOURCE DOCUMENT: SEER/Tumor Registry, otherwise medical record: pathology report.

CODE RANGE: 01-03

DIRECTIVES: If immunohistochemistry (IHC) is used then code 01.
If florescent in situ hybridization is used then code 02.
If both tests were used then code 03.

4 Non-Surgical Treatments for Breast Cancer

4.1 *Discussion of radiation therapy*

DATA ELEMENT: Discussion about radiation therapy

DEFINITION: Did the patient's surgeon discuss radiation therapy with her?

SOURCE DOCUMENT: Medical record.

CODE RANGE: 01 – 02

DIRECTIVES: If there is definite mention that the patient's doctor discussed radiation therapy with her then code 01.
If there is no mention of a discussion between the patient and her doctor about radiation therapy then code as 02.

4.1.1 Receipt of radiation treatment

DATA ELEMENT:	Receipt of radiation therapy
DEFINITION:	Given that the patient was referred to a radiation oncologist did they receive radiation therapy?
SOURCE DOCUMENT:	Medical record.
CODE RANGE:	01 – 04
DIRECTIVES:	<p>If the patient had any radiation therapy code 01.</p> <p>If the radiation oncologist recommended radiation therapy but the patient refused, code 02 and skip to 4.2.</p> <p>If the radiation oncologist did not recommend radiation therapy for the patient, code 03 and skip to 4.2</p> <p>If there is no mention in the record of radiation therapy, code 04 and skip to 4.2</p>

4.1.2 Completion of radiation therapy

DATA ELEMENT:	Completion of radiation therapy
DEFINITION:	Was the number of sessions that the patient received considered a complete series?
SOURCE DOCUMENT:	Medical record.
CODE RANGE:	01 – 09
DIRECTIVES:	<p>If there is mention that the radiation therapy was completed code 01</p> <p>If the series of radiation therapy was not complete code 02</p> <p>If it is unknown whether the series was complete code 09</p>

4.2 Discussion of chemotherapy

DATA ELEMENT:	Discussion about chemotherapy
DEFINITION:	Did the patient's surgeon or radiation oncologist discuss radiation therapy with her?
SOURCE DOCUMENT:	Medical record.
CODE RANGE:	01 – 02
DIRECTIVES:	If there is definite mention that the patient's doctor discussed any aspect of chemotherapy with her then code 01. If there is no mention of a discussion about chemotherapy but the patient was referred to a medical oncologist then code 01.

If there is no mention of a discussion between the patient and her doctor about chemotherapy then code as 02.

4.2.1 Receipt of chemotherapy

DATA ELEMENT:	Receipt of chemotherapy
DEFINITION:	Given that the patient was referred to a medical oncologist did they receive chemotherapy (intravenous and / or p.o.)?
SOURCE DOCUMENT:	Medical record.
CODE RANGE:	01 – 04
DIRECTIVES:	<p>If the patient had any chemotherapy code 01.</p> <p>If the medical oncologist recommended chemotherapy but the patient refused, code 02 and skip to 4.3.</p> <p>If the medical oncologist did not recommend chemotherapy for the patient, code 03 and skip to 4.3.</p> <p>If there is no mention in the record of chemotherapy, code 04 and skip to 4.3.</p>

4.2.2 Type of chemotherapy

DATA ELEMENT:	Type of chemotherapy received
DEFINITION:	The proprietary drug name of the chemotherapeutic received.
SOURCE DOCUMENT:	Medical oncologist's report, medical record.
CODE RANGE:	Y/N
DIRECTIVES:	<p>For each chemotherapeutic listed indicate whether or not the patient received the drug.</p> <p>If the patient received a drug not included in the list indicate using the other category and specify the drug. If a patient was enrolled in a clinical trial then specify under other.</p>

4.2.3 Completion of chemotherapy

DATA ELEMENT:	Completion of chemotherapy
DEFINITION:	Was the number of courses that the patient received considered a complete series?
SOURCE DOCUMENT:	Medical oncologist's report, medical record.
CODE RANGE:	01 – 09
DIRECTIVES:	If there is mention that the chemotherapy was completed code 01

If the series of chemotherapy was not complete code 02.

If it is unknown whether the series was complete code

4.3 Receipt of Biotherapy

DATA ELEMENT:	Receipt of biotherapy
DEFINITION:	Did the patient receive biotherapy?
SOURCE DOCUMENT:	Medical record.
CODE RANGE:	01 – 05
DIRECTIVES:	<p>If the patient had any biotherapy code 01.</p> <p>If a physician recommended therapy but the patient refused, code 02 and.</p> <p>If a physician did not recommend therapy for the patient, code 03 and skip to 5.</p> <p>If there is no mention in the record of therapy, code 04 and skip to 5.</p> <p>If the patient is enrolled in a blinded clinical trial involving therapy and details regarding therapy are unknown then code as 05 and skip to 5.</p>

4.4 Type of biotherapy

DATA ELEMENT:	Type of biotherapy received
DEFINITION:	The drug name of the biotherapeutic agents received.
SOURCE DOCUMENT:	Medical oncologist's report, medical record.
CODE RANGE:	Y/N
DIRECTIVES:	<p>For each biotherapeutic agent listed indicate whether or not the patient received the drug.</p> <p>If the patient received a drug not included in the list indicate use the other category and specify the drug.</p> <p>If there is no mention of a drug in the medical record then code as 'No'.</p>

5 Breast cancer recurrence

5.1 *Did the patient have a recurrence?*

DATA ELEMENT:	Screening question for recurrence
DEFINITION:	Determines whether the patient has been diagnosed with a recurrence.
SOURCE DOCUMENT:	Medical record
CODE RANGE:	01 – 02
DIRECTIVES:	Required. We will define a recurrence as a tumor that is found after four months of the original diagnosis or through completion of surgery(ies) in first course of treatment, whichever is longer. Do not include ductal carcinoma in-situ or the diagnosis of any other non-invasive tumor as a recurrence Code 01 if there is a definite indication of a breast cancer recurrence. Go to 5.1.1. If there is no mention that the patient had a recurrence then code 02 and skip to 7.

5.1.1 Side of recurrence

DATA ELEMENT:	Side of breast cancer recurrence.
DEFINITION:	The anatomic side (left or right) where the breast cancer recurrence occurred
SOURCE DOCUMENT:	Medical record
CODE RANGE:	01– 02.
DIRECTIVES:	01 = left (the breast cancer recurrence is in the left breast) 02 = right (the breast cancer recurrence is in the right breast)

5.1.2 Was the recurrence considered a second primary?

DATA ELEMENT:	Recurrence
DEFINITION:	Clarification of recurrence
SOURCE DOCUMENT:	Medical record
CODE RANGE:	01– 02.
DIRECTIVES:	01 = Yes

02 = No

5.2 Method of diagnosis

DATA ELEMENT: Method of recurrence diagnosis

DEFINITION: Was the recurrence diagnosed pathologically or clinically?

SOURCE DOCUMENT: Medical Record

CODE RANGE: 01 – 02

DIRECTIVES: If the diagnosis was based on tissue (histology) then code as 01 and go to 5.2.1.

If the diagnosis was based on any other method including physical examination, mammography, ultrasound, x-ray, CT scan, or MRI code as 02 and go to 5.2.2.

5.2.1 Date of pathological diagnosis

DATA ELEMENT: Date of pathological diagnosis

DEFINITION: The date of a pathological diagnosis of a breast cancer recurrence.

SOURCE DOCUMENT: Medical Record

CODE RANGE: Record as MONTH, DAY, YEAR (MM / DD / YYYY)
MONTH 01-12,99
DAY 01-31,99
YEAR 1996 – 2006. Code complete (4-digit) year.

DIRECTIVES: Required.

5.2.2 Date of clinical diagnosis

DATA ELEMENT: Date of clinical diagnosis

DEFINITION: The date of a clinical diagnosis of a breast cancer recurrence.

SOURCE DOCUMENT: Medical Record

CODE RANGE: Record as MONTH, DAY, YEAR (MM / DD / YYYY)
MONTH 01-12,99
DAY 01-31,99
YEAR 1996 – 2006. Code complete (4-digit) year.

DIRECTIVES: Required.

5.3 *Location of breast cancer recurrence:*

DATA ELEMENT:	Location of breast cancer recurrence.
DEFINITION:	Characterization of the breast cancer recurrence as local, regional, or distant.
SOURCE DOCUMENT:	Medical record
CODE RANGE:	Y / N
DIRECTIVES:	<p>For each of the three possible locations, check yes or no.</p> <p>Check yes for local if the recurrence is in the breast. Otherwise, check no.</p> <p>Check yes for regional if the breast cancer spread to the lymph nodes, skin, or chest muscle on the side of the original tumor. Otherwise, check no.</p> <p>Check yes for distant if the breast cancer spread outside of the breast or axilla (<i>e.g.</i>, to bone, brain, lung, or other organs). Otherwise, check no.</p>

6 Death

6.1 *Is the patient deceased?*

DATA ELEMENT:	Screening question for death of patient
DEFINITION:	Determines whether the patient has died
SOURCE DOCUMENT:	Medical record
CODE RANGE:	01 – 03
DIRECTIVES:	<p>If the patient is reported as having died then code 01.</p> <p>If the patient is alive at the last medical contact then code 02.</p>

6.2Date of death

DATA ELEMENT:	Date
DEFINITION:	Date of death
SOURCE DOCUMENT:	Medical record
CODE RANGE:	<p>Record as MONTH, DAY, YEAR (MM / DD / YYYY)</p> <p>MONTH 01-12,99</p> <p>DAY 01-31,99</p> <p>YEAR 1996 – 2006. Code complete (4-digit) year.</p>
DIRECTIVES:	If the medical record indicates that the patient has died but the exact date of death is unknown then code as 99/99/9999.

6.3 *Cause of Death*

DATA ELEMENT:	Cause of death
DEFINITION:	Reason for death recorded in the medical record
SOURCE DOCUMENT:	Medical record
CODE RANGE:	None
DIRECTIVES:	Record the text from the medical record that describes the patient's cause of death.

6.4Date of last known encounter

DATA ELEMENT:	Date
DEFINITION:	Date of last encounter with the medical system
SOURCE DOCUMENT:	Medical record
CODE RANGE:	Record as MONTH, DAY, YEAR (MM / DD / YYYY) MONTH 01-12,99 DAY 01-31,99 YEAR 1996 – 2006. Code complete (4-digit) year.
DIRECTIVES:	Required. Date of last medical encounter that the patient had with the system.

6.4.1 Poor prognosis at last encounter?

DATA ELEMENT:	Short-term expected prognosis
DEFINITION:	Short-term expected prognosis
SOURCE DOCUMENT:	Medical Record
CODE RANGE:	Y/N
DIRECTIVES:	Required.

APPENDIX B – DATA COLLECTION INSTRUMENT

Significance of Pathways Leading to RhoC Overexpression in Breast Cancer

Data Collection Instrument (DCI)

E1 Eligibility Information

E1.1 Date of Diagnosis (MM/DD/YYYY): __ __/__ __/__ __ __ __

If month is unknown enter MM = 06. If day is unknown enter DD = 15.

E1.2 Was the tumor an invasive malignancy? __ __ (enter code from below)

01 = Yes go to E1.3

02 = No – **Ineligible (end of data collection)**

09 = Unknown – **for review**

E1.3 Was the cancer bilateral? __ __ (enter code from below)

01 = Yes – **Ineligible (end of data collection)**

02 = No go to E1.4

E1.3.1 Side of breast cancer: __ __ (enter code from below)

01 = Right

02 = Left

E1.4 What stage is the tumor? __ __

(T = ____, N = ____, M = ____)

00 = Stage 0 - **Ineligible (end of data collection)**

01 = Stage I – (T1, N0, M0)

02 = Stage IIA – (T0, N1,M0; T1, N1,M0; T2, N0, M0)

03 = Stage IIB – (T2, N1, M0; T3, N0, M0)

04 = Stage III – **Ineligible (end of data collection)**

05 = Stage IV – **Ineligible (end of data collection)**

09 = Unknown – **Ineligible (end of data collection)**

E1.5 Source of stage information: __ __ (enter code from below)

The following list of options is arranged in order from the most important (00) to the least important (06). Select the first and therefore most important from this list that is the source of the above stage information.

- 00 = Pathology report
- 01 = Pathology report, referred to but not in the chart
- 02 = Surgery notes
- 03 = MD notes from hematology/oncology
- 04 = MD notes, primary care physician
- 05 = MD notes, other
- 06 = Other, specify: _____

E1.6 Is it the woman's first episode of malignant breast cancer?: __ __

(enter code from below)

- 01 = Yes go to E1.7
- 02 = No – **Ineligible (end of data collection)**

E1.7 Was the woman diagnosed with any other clinically active malignancy at the time of her breast cancer diagnosis? __ __ (enter code from below)

- 01 = Yes – **Ineligible (end of data collection)**
- 02 = No

E1.8 Age at diagnosis: __ __ __ Years (enter up to 3 digit age in years)

1.0 Demographic Information

1.1 Patient's ID: __ __ __ __

1.2 Date of Birth (MM/YYYY): __ __ / __ __ __ __

If month is unknown enter MM = 06.

1.3 Ethnicity: __ __ (enter code from below)

- 00 = Not Hispanic or Latino
- 01 = Hispanic or Latino
- 09 = Unknown

1.4 Race: __ __ (enter code from below)

- 01 = White
- 02 = African – American
- 03 = Arab (specify _____)

04 = Other (specify _____)

2.0 Personal History

2.1 Medical History

<i>Condition</i>	<i>Yes</i>	<i>No</i>	<i>Specify</i>
Prior cancer (excluding breast & non-melanoma)	X	X	
Heart disease (MI, CAD, CHF, etc)	X	X	
Cerebrovascular disease (Stroke)	X	X	
Hypertension	X	X	
Hypercholesterolemia	X	X	

2.2 Family History

<i>Cancer</i>	<i>Yes</i>	<i>No</i>	<i>1st degree</i>	<i>Non-1st degree</i>
Breast	X	X	X	X
Ovarian	X	X	X	X
Other: Specify:	X	X	X	X
Other: Specify:	X	X	X	X
Other: Specify:	X	X	X	X

2.3 Has she been diagnosed with *in situ* disease?

		LCIS	DCIS	No
2.3.1	Prior to invasive diagnosis	X	X	X
2.3.2	Simultaneous with invasive diagnosis	X	X	X
2.3.3	After invasive diagnosis but prior to recurrent invasive disease	X	X	X

2.4 Smoking status: ____ (enter code from below)

01 = Former smoker
 02 = Current smoker
 03 = Never smoked
 04 = Unknown

2.5 Marital Status: ____ (enter code from below)

01 = Married
 02 = Divorced/Widowed

03 = Separated/single/never married
04 = Unknown

2.6 Gravity: __ __

00 = No pregnancies (skip to 2.8)
99 = No mention

2.7 Parity: __ __

00 = No live births (skip to 2.8)
99 = No mention

2.8 Age of first live birth: __ __ Years

2.9 Age at menarche: __ __ Years

2.10 Age at menopause: __ __ Years

00 = Not menopausal **skip to 2.13**
01 = Perimenopausal **skip to 2.13**

2.11 Type of menopause: __ __

01 = Natural
02 = Surgical
03 = Chemical/Drugs/Chemotherapy
04 = No mention

2.12 History of use of hormone replacement therapy? __ __ (enter code from below)

01 = Yes
02 = No
03 = Unknown

2.13 History of oral contraceptive (OC) use? __ __ (enter code from below)

01 = Yes
02 = No
03 = Unknown

2.14 Weight at time of diagnosis? __ __ __

2.14.1 Weight units: __ __ (enter code from below)

01=pounds
02=kilograms

2.15 Height at diagnosis? ____ ____ ____ ____

2.15.1 Height units: ____ ____ (enter code from below)

01=inches (“ or in)

02=cm

3.0 Breast Cancer Abstract

3.1 Tumor size

3.1.1 Is a tumor size reported?: ____ ____ (enter code from below)

01 = Yes (skip to 0)

02 = No (skip to 0)

3.1.2 Tumor size in largest dimension
(add up largest dimensions of all pieces of largest tumor)

____ ____ ____ ■ ____ ____

3.1.3 Tumor size units: ____ ____ (enter code from below)

01 = Centimeters (cm)

02 = Millimeters (mm)

03 = Inches (in. or “)

04 = Other units; specify _____

3.2 Histology: ____ ____ (enter code from below)

Codes for Histology

01 = Infiltrating ductal carcinoma (ICD-O code 8500)

02 = Infiltrating lobular carcinoma (ICD-O codes 8520 or 8521)

03 = Infiltrating ductal and lobular carcinoma (ICD-O code 8523)

04 = Carcinoma, Unspecified (ICD-O code 8010)

05 = Adenocarcinoma, unspecified, mucinous or tubular (ICD-O codes 8140, 8211, or 8480)

06 = Other (specify) _____

99 = Pathology unknown

3.3 Histologic grade: ____ ____ (enter code from below)

Codes for histologic grade:

01 = Grade 1 (well differentiated)

02 = Grade 2 (intermediate or moderately differentiated)

03 = Grade 3 (poorly differentiated)

04 = Grade 4 (undifferentiated, anaplastic)

09 = Cell type not determined or not stated

3.4 Definitive breast surgical procedure: ____ ____ (enter code from below)

00 = Lumpectomy/Biopsy

10 = Partial / less than total mastectomy without dissection of axillary lymph nodes

20 = Partial / less than total mastectomy with dissection of axillary nodes

- 30 = Subcutaneous mastectomy with / without dissection of axillary nodes
 40 = Total (simple) mastectomy (breast only) without dissection of axillary lymph nodes
 50 = Modified radical / total (simple) mastectomy (may include portion of pectoralis major) with dissection of axillary lymph nodes
 60 = Radical mastectomy with dissection of majority of pectoralis major with dissection of axillary lymph nodes
 70 = Extended radical mastectomy (code 60 plus internal mammary node dissection; may include chest wall and ribs)
 80 = Mastectomy NOS
 90 = No surgery mentioned
 98 = Enrolled in clinical trial, surgical procedure unknown

3.5 Date of definitive surgery (MM/DD/YYYY): ____ / ____ / ____
 If month is unknown enter MM = 06. If day is unknown enter DD = 15.

3.5.1 Pathology number for surgery: S ____ - ____

3.6 In the final surgical report were the margins histologically clear of malignancy? ____ (enter code from below)

- 01 = Yes (go to 3.7)
 02 = No
 03 = Pathology report does not have sufficient information (go to 3.7)

3.7 What type of malignancy was present at the margins? (circle yes or no for each item)

	Yes	No
Invasive cancer	X	X
In-situ cancer	X	X

3.8 All other surgeries

Date of surgery	Surgery Type (enter code) 01 = biopsy 02 = re-excision 03 = axillary node dissection	Pathology Number	Contents: (circle one) Yes No	
____ / ____ / ____	____	S ____ - ____	Tumor: X	X
			Lymph nodes: X	X
____ / ____ / ____	____	S ____ - ____	Tumor: X	X
			Lymph nodes: X	X

___ / ___ / ___	___	S ___ - ___	Tumor: X X Lymph nodes: X X
___ / ___ / ___	___	S ___ - ___	Tumor: X X Lymph nodes: X X
___ / ___ / ___	___	S ___ - ___	Tumor: X X Lymph nodes: X X

3.8 Axillary node evaluation

3.8.1 Is there a report of axillary node evaluation? ___ (enter code from below)

- 01 = Yes, there is definitive mention of axillary node evaluation
02 = Yes, there is definitive mention of sentinel node evaluation
03 = No, record indicates that there was no axillary node evaluation (skip to 3.8)
09 = Unknown, record contains no mention of axillary node evaluation (skip to 3.8)

3.8.2 How many nodes were examined: ___ (enter total from all procedures)

3.8.3 How many nodes were positive: ___ (enter total from all procedures)

3.9 Estrogen receptor protein: ___ (enter code from below)

- Estrogen receptor protein codes:
- 00 = Test not done (documented)
 - 01 = Positive test result
 - 02 = Negative test result
 - 03 = Borderline/indeterminate/sub-optimal test result
 - 08 = Ordered but results not in chart
 - 09 = Unknown or no information

3.10 Progesterone receptor protein: ___ (enter code from below)

- Progesterone receptor protein codes:
- 00 = Test not done (documented)
 - 01 = Positive test result
 - 02 = Negative test result
 - 03 = Borderline/indeterminate/sub-optimal test result
 - 08 = Ordered but results not in chart
 - 09 = Unknown or no information

3.11 Her2/neu Status: ___ (enter code from below)

- Her2/neu codes:
- 00 = Test not done (cases <1999) **skip to 4**
 - 01 = 1+
 - 02 = 2+
 - 03 = 3+
 - 04 = negative

08 = Ordered but results not in chart
09 = Unknown or no information

3.11.1 Her2/neu Test type: __ __

01 = IHC
02 = FISH
03 = Both

4.0 Non-Surgical Treatments for Breast Cancer

4.1 Was radiation treatment discussed? __ __ (enter code from below)

01 = Yes
02 = No

4.1.1 Radiation treatment: __ __ (enter code from below)

01 = Patient received radiation therapy
02 = Patient refused radiation therapy (skip to 0)
03 = Radiation oncologist did not recommend radiation therapy (skip to 0)
04 = No information in record about radiation therapy (skip to 0)

4.1.2 Was the series considered complete? __ __ (enter code from below)

01 = Yes
02 = No
09 = Unknown

4.2 Was chemotherapy discussed? __ __ (enter code from below)

01 = Yes
02 = No

4.2.1 Chemotherapy: __ __ (enter code from below)

01 = Patient received chemotherapy
02 = Patient refused chemotherapy (skip to 4.3)
03 = Medical oncologist did not recommend chemotherapy (skip to 4.3)
04 = No information in record about chemotherapy (skip to 4.3)

4.2.2 Type of chemotherapy received: (circle applicable answer for each item)

Yes No

Cyclophosphamide (Cytosan)	X	X
Methotrexate	X	X
5-Fluorouracil (5-FU)	X	X
Doxorubicin or Epirubicin	X	X
Docetaxel or Paclitaxel	X	X
Capecitabine	X	X
Vinorelbine or Gemcitabine	X	X
Other specify:	X	X

4.2.3 Was the series considered complete? __ __ (enter code from below)

- 01 = Yes (skip to 4.3)
02 = No
09 = Unknown (skip to 4.3)

4.3 Biotherapy: __ __ (enter code from below)

- 01 = Patient received biotherapy
02 = Patient refused therapy **skip to 5**
03 = Physician did not recommend therapy **skip to 5**
04 = No information about therapy **skip to 5**
05 = Patient is enrolled in clinical trial, details regarding therapy are unknown **skip to 5**

4.4 Type of biotherapy received: (circle applicable answer for each item)

	Yes	No
<i>4.4.1 Herceptin</i>	X	X
<i>4.4.2 Tamoxifen</i>	X	X
<i>4.4.3 Aromatase Inhibitor</i>	X	X
<i>4.4.4 Other (specify)</i>	X	X

5.0 Breast cancer recurrence

5.1 Did the patient have a recurrence? __ __ (enter code from below)

01 = Yes

02 = No (go to 6)

5.1.1 Side of recurrence: __ __ (enter code from below)

01 = Left

02 = Right

5.1.2 Was this considered a second primary: __ __ (enter code from below)

01 = Yes

02 = No

5.2 Was the recurrence diagnosed pathologically? __ __ (enter code from below)

01 = Yes (go to 0)

02 = No (go to 0)

5.2.1 Date of pathological diagnosis (MM/DD/YYYY): __ __ / __ __ / __ __ __ __

Go to 5.3 If month is unknown enter MM = 06. If day is unknown enter DD = 15.

5.2.2 Date of clinical diagnosis (MM/DD/YYYY): __ __ / __ __ / __ __ __ __

If month is unknown enter MM = 06. If day is unknown enter DD = 15.

5.3 Location of breast cancer recurrence:
(circle applicable answer for each item)

Yes

No

5.3.1 Local (The recurrence is in the breast on the side of the original tumor.) X X

5.3.2 Regional (The recurrence has spread to the lymph nodes, skin, or chest muscle on the side of the original tumor.) X X

5.3.3 Distant (There has been metastatic spread outside of the breast or axilla, *e.g.*, to bone, brain, lung, or other organs.) X X

5.3.4 Site of distant metastasis (There has been metastatic spread outside of the breast or axilla, *e.g.*, to bone, brain, lung, or other organs- specify site below)

6.0 Death

6.1 Is subject deceased? ____ (enter code from below)

01 = Yes (go to 6.2)

02 = No (go to 6.4)

6.2 Date of death: ____ / ____ / ____

6.3 Cause(s) of death:

6.4 Date of last encounter: ____ / ____ / ____

6.4.1 Was patient prognosis poor at last encounter? (Y/N) _____